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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,261	07/06/2006	Francis J. Michon	13564-105030	3361

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EXAMINER	
ARCHIE, NINA	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
10/26/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/562,261	MICHON, FRANCIS J.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 4-5, 7-9, 11-16, and 29-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,7-9,11-16,29 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/13/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 4, 2010 has been entered.

Amendment Entry

2. The amendment filed March 4, 2010 has been entered. Claims 1, 4-5, 7-9, 11-16, and 18-30 are pending. Claims 1, 13, 18-22, and 30 has been amended. Claims 18-28 are withdrawn as being drawn to non-elected inventions. Claims 1, 4-5, 7-9, 11-16 and 29-30 are currently under examination.

Information Disclosure Statement

3. The information disclosure statement filed on 9/13/2010 has been considered. An initialed copy is enclosed.

Withdrawal of Rejection

4. The rejection of claims 1, 4-5, 7-9, 11-16, and 29-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Costantino WO 2003/007985 Date January 30, 2003 in view of Porro et al US 20060165730 (US Filing Date May 7, 2003), and Michon et al WO 2000/10599 Date March 2, 2000, and Michon et al WO 2000/10599 Date March 2, 2000 has been withdrawn in light of applicant's amendment thereto. It should be noted that said amendment introduces new matter limitations. Therefore, the rejection maybe reinstated depending on the resolution of the new matter issue set forth below.

Response to Arguments

5. Applicant's arguments with respect to claims 1, 4-5, 7-9, 11-16 and 29-30 have been considered but are moot in view of the ground(s) of rejection.

New Grounds of Rejection

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 4-5, 7-9, 11-16, and 29-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

As to independent claim 1 and 30, and dependent claims 4-5, 7-9, 11-16, and 29, said claims specifically reciting the limitation "wherein the group Y meningococcal polysaccharide fragment is completely N-acetylated and wherein the carrier protein is covalently coupled to the group Y meningococcal polysaccharide fragment at the de-O-acetylation sites" and specifically reciting the limitation "wherein said polysaccharide is selected from the group consisting of an O-acetyl negative group Y and a fragment of an O-acetyl positive group Y meningococcal polysaccharide, wherein the fragment of an O-acetyl positive group Y meningococcal is completely N-acetylated, wherein the carrier protein is covalently coupled to the polysaccharide at the de-O-acetylation sites". The limitation is not provided for in the specification as originally filed. Applicant filed a statement in the Applicants Arguments/Remarks on 3/4/2010 stating support for the amendment that can be found in paragraphs [0666-0668] of the specification as filed. Applicant has not provided support in the specification specifically for the recitations aforementioned above. Even though the specification discloses partial deacetylation, there is no support provided in the written description of the specification stating specifically the limitation "wherein the group Y meningococcal polysaccharide fragment is completely N-acetylated and wherein the carrier protein is covalently coupled to the group Y meningococcal polysaccharide fragment at the de-O-acetylation sites" and specifically reciting the limitation "wherein said polysaccharide is selected from the group consisting of an O-acetyl negative group Y and a fragment of an O-acetyl positive group Y meningococcal polysaccharide, wherein the fragment

of an O-acetyl positive group Y meningococcal is completely N-acetylated, wherein the carrier protein is covalently coupled to the polysaccharide at the de-O-acetylation sites" as directed to the claims. Therefore, it is apparent, that Applicants were not in possession of the claimed liposome at the time of filing. Applicants pointing to the specification by page and line number where specific written description for said recitation set forth supra may resolve this issue. This is a new matter rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 4-5, 7-9, 11-16, and 29-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) As to independent claims 1, 11, and 30 and dependent claims 4, 5, 7-9, 11-16, and 29 reciting the limitation "less than about" is relative which renders the claim indefinite. The recitation "less than about" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

b) As to dependent claim 29, the claims do not recite an article such as "the." The claims therefore encompass any immunogenic conjugate, but then attempt to limit the immunogenic conjugate of independent claim 1. Amendment of the claims to add the word "The" would obviate this issue.

35 USC §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill

in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1, 4-5, 7-9, 11-16, and 29-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over (Costantino WO 2003/007985 Date January 30, 2003) in view of (Porro et al US Application No. 20060165730 (US Filing Date May 7, 2003)), and (Michon et al US Application 20040213804A1 US Filing Date January 20, 2004 (parent continuation-of 09376911 Date August 18, 1998.

The instant claims are drawn to an immunogenic conjugate comprising a carrier protein, and a group Y meningococcal polysaccharide fragment obtained from an O-acetyl positive group Y meningococcal polysaccharide, wherein the group Y meningococcal polysaccharide fragment has a molecular weight less than about 150 kDa and has been O-deacetylated by at least 80%, and is completely N-acetylated; wherein the carrier protein is covalently coupled to the group Y meningococcal polysaccharide fragment at the de-O-acetylation sites; and wherein the immunogenic conjugate is suitable for use as a vaccine against N. meningitidis infection (claim 1), wherein the group Y meningococcal polysaccharide fragment has a molecular weight from about 2.5 kDa to about 100 kDa (claim 4), wherein the group Y meningococcal polysaccharide fragment has a molecular weight from about 10 kDa to about 20 kDa (claim 5), wherein the carrier protein is a bacterial toxin or toxoid (claim 7), wherein the bacteria toxin or toxoid is selected from the group consisting of diphtheria, tetanus, pseudomonas, staphylococcus, streptococcus, pertussis and Escherichia coli toxin or toxoid (claim 8), wherein the bacterial toxin or toxoid is tetanus toxin or toxoid (claim 9); a vaccine comprising the immunogenic conjugate (claim 11), wherein the bacterial toxin or toxoid is selected from the group consisting of diphtheria, tetanus, pseudomonas, staphylococcus, streptococcus, meningococcal porin B, pertussis and Escherichia coli toxin or toxoid (claim 12), wherein the bacterial toxin or toxoid is tetanus toxin or toxoid (claim 13), further comprising an adjuvant (claim 14), wherein the adjuvant is aluminum hydroxide (claim 15), wherein the vaccine is adapted for administration by

injection (claim 16), wherein the group Y meningococcal polysaccharide fragment is 100% O-deacetylated (claim 29); an immunogenic conjugate comprising a carrier protein, and a polysaccharide, wherein said polysaccharide is selected from the group consisting of an O-acetyl negative group Y and a fragment of an O-acetyl positive group Y meningococcal polysaccharide, wherein the fragment of an O-acetyl positive group Y meningococcal polysaccharide has a molecular weight in the range of about 5 to about 150 kDa, has been O-deacetylated by at least 80%, and is completely N-acetylated, wherein the carrier protein is covalently coupled to the polysaccharide at the de-O-acetylation sites; and wherein the immunogenic conjugate is suitable for use as a vaccine against N. meningitidis infection (claim 30).

Costantino teach vaccine and immunogenic compositions comprising capsular saccharides from serogroups Y of N. meningitidis, wherein said capsular saccharides are conjugated to carrier protein (s) and/or are oligosaccharides. Constantino et al teach the material obtained (fragment) can be conjugated to a carrier protein and formulated as a vaccine (see abstract, claims). Constantino teach MenY 242975 (OAc-) and 240539 (OAc+)[i.e. O-acetyl positive/negative group Y] (see pg. 19 lines 10-15) ultrafiltered to produce a molecular weight of 30kDa (see pg. 14 lines 1-10 and pg. 15 b and c) which necessarily teach a polysaccharide fragment that has a molecular weight less than about 150 kDa. Constantino et al teach carrier proteins that are bacterial toxins or toxoids, such as diphtheria or tetanus toxoids (see pg. 4 lines 15-20). Constantino et al teach a vaccine may include an adjuvant to enhance effectiveness of the composition which include, aluminum salts (alum), such as aluminum hydroxides (see claims 61-63).

Thus the immunogenic conjugate of Constantino necessarily teach a group Y meningococcal polysaccharide fragment obtained from and O-acetyl positive group Y meningococcal polysaccharide, wherein said polysaccharide of an O-acetyl negative group Y or a fragment of an O-acetyl positive group Y meningococcal polysaccharide, wherein the group Y meningococcal polysaccharide of an O-acetyl positive group fragment has a molecular weight less than about 150 kDa and has been O-deacetylated by at least 80%, wherein the carrier protein is covalently coupled to the group Y meningococcal polysaccharide fragment, is completely N-acetylated, wherein the immunogenic conjugate is suitable for use as a vaccine against N. meningitidis infection, wherein the group Y meningococcal polysaccharide fragment has a

molecular weight from about 2.5 kDa to about 100 kDa, wherein the group Y meningococcal polysaccharide fragment has a molecular weight from about 10 kDa to about 20 kDa.

Constantino does not teach an immunogenic conjugate, and wherein the group Y meningococcal polysaccharide fragments has been O-deacetylated by at least 80%, wherein group Y meningococcal polysaccharide fragment is completely N-acetylated, wherein the carrier protein is covalently coupled to the group Y meningococcal polysaccharide fragment at the de-O-acetylation sites.

Porro et al teach that "Ps structure are conveniently represented by the O-acetyl free oxidryl residues" and that "de-O-acetylation can be selectively and quantitatively achieved therefore Porro et al anticipate the degree of de-O-acetylation is greater than 80%, for use as a vaccine against N. meningitidis infection (see paragraphs [0025] and [0027]). Porro et al teach an immunogenic conjugate comprising group Y meningococcal polysaccharide covalently coupled to polymeric carrier, including O-deacetylated O-acetyl-positive group Y meningococcal polysaccharide or a fragment thereof, wherein the degree of de-O-acetylation, characterized in the degree of de-O-acetylation is 100% (see abstract, claims, see paragraphs [0025] and [0027], steps 1-4). Porro et al teach a conjugate product comprising a de-O-acetylated meningococcal Y polysaccharide conjugated to a carrier protein, wherein the carrier protein is a bacterial toxin or toxoid, wherein the bacteria toxin or toxoid is tetanus (see paragraph [0043]), wherein the modified meningococcal Y polysaccharide is as defined in claim 2. Porro et al teach a vaccine, wherein the bacterial toxin or toxoid is tetanus, which comprises an adjuvant, wherein the adjuvant is aluminum hydroxide (see paragraphs [0061]-[0062], which is adapted for administration by injection, wherein the conjugated material comprises a polysaccharide as defined in claim 2 (see abstract, claims).

Michon et al teach an immunogenic polysaccharide-protein conjugate directly coupled to a protein through beta.-position sites of one or more propionate moieties of the N-propionated polysaccharide or N-propionated oligosaccharide; wherein the N-propionated polysaccharide is directly coupled to the protein elicits protective antibodies reactive with the N-propionated polysaccharide, wherein the N-propionated polysaccharide comprises de-N-acetylation of a polysaccharide by base or enzymatic hydrolysis followed by N-deacetylated polysaccharide. Michon et al teach a base for effective hydrolysis of all or a part of the N-acyl groups in the

polysaccharide such as Neisseria meningitides group type Y polysaccharide (see paragraph [0052]). Michon et al teach a wide variety of conditions can be used for hydrolysis of the polysaccharide in either aqueous or organic solvent according to the invention by methods known in the art. In one embodiment, at least about 50% of the N-acetyl groups are removed by hydrolysis, preferably about 50% to about 100% are removed, more preferably about 95% or more of the native N-acetyl groups are removed and the N-acetyl groups are hydrolyzed from the polysaccharide by treatment with a hydrolysis reagent (see paragraph [0030]).

It would have been prima facie obvious at the time the invention was made to modify a group Y meningococcal polysaccharide fragments obtained from an O-acetyl positive group Y meningococcal polysaccharide conjugate as taught by Constantino and further undergo deacetylation in polysaccharide fragments by at least 80% in order to covalently couple said polysaccharide fragments at de-O-acetylation sites to a carrier protein as taught by Porro et al. In order to take advantage of activating "selected regions" that are O-acetyl free which leads to reactive amino groups in the selected regions of the Ps structure allowing direct conjugation (see paragraph [0025]) of a given protein carrier, wherein the activation does not limit the yield of reactions which form direct conjugation and does not penalize the sterical hindrance of two large molecules (i.e. Ps and the Protein) that must interact (see paragraphs [0024]-[0025]).

It would have been prima facie obvious at the time the invention was made to modify a group Y meningococcal polysaccharide fragments obtained from an O-acetyl positive group Y meningococcal polysaccharide conjugate as taught by Constantino wherein group Y meningococcal polysaccharide fragments undergoes complete N-acetylation and is conjugated to a carrier protein as taught by Michon et al in order to take advantage of linking conjugate molecules (i.e. Ps and carrier Protein) through one or more sites on the polysaccharide (see [0051]) and not altering the charged functional group which often interacts with/or forms part of the epitope that is crucial for immunity (see paragraphs [0052]-[0056]) in a polysaccharide conjugate.

As to claims 1 and 16, to the limitation “use as a vaccine against N. meningitidis infection”, “wherein the vaccine is adapted for administration by injection”, said recitations are considered an intended use and thus is given no patentable weight on the conjugate. Therefore the claims are drawn to a conjugate.

One would have reasonable expectation of success because O-acetyl positive group Y meningococcal polysaccharide from Neisseria meningitides group type Y polysaccharide to produce an immunogenic conjugate is well known in the art.

Conclusion

9. No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nina A Archie
Examiner
GAU 1645
REM 3B31

/Robert A. Zeman/

for Nina Archie, Examiner of Art Unit 1645